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EXAMINER	
JAVANMARD, SAHAR	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/519,793	JOHN, VARGHESE	
	Examiner	Art Unit	
	SAHAR JAVANMARD	4133	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 20* is/are pending in the application.

4a) Of the above claim(s) *9 and 11-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/ are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *23 December 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Office Action is in response to the 371 of PCT/US03/20383 filed June 27, 2003. Claims 7, 8, 10, and 15-19 have been cancelled. Amended claims 1-6, 9, 11-14, 20 are being examined on the merits herein.

Status of the Claims

This Office Action is in response to Applicant's remarks filed on 12/20/2007. Claim(s) 1-6, 9, 11-14, and 20 are pending. Claim(s) 9, and 11-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claims 7-8, 10, 15-19, and 21-22 have been cancelled. Applicant's election of species of a disease (Alzheimer's disease) and compound (benzyl (S)-1-((2S, 3S, 5R)-3-hydroxy- 5-(5-isobutyryl-1H-imidazol-2-yl)-1,6-diphenylhexan-2-ylamino)- 3-methyl-1-oxobutan-2-ylcarbamate) without traverse of the restriction requirement in the reply is acknowledged. The requirement is deemed proper and is therefore made FINAL. Claim(s) 1-6 and 20 are examined herein insofar as they read on the elected invention and species.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating Alzheimer's disease in a human patient, does not reasonably provide enablement for a method of preventing Alzheimer's disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The claims are directed to a method of treating or preventing Alzheimer's disease in a human by administering compounds of formula I. The specification fails to adequately teach how to use the herein claimed method of preventing Alzheimer's disease in a human.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The Nature of the Invention:

The rejected claims are drawn to a method of treating or preventing Alzheimer's, comprising administering an effective amount of compounds of formula I.

(2) Breadth of the Claims:

The instant claims embrace a variety of inhibitors of cell cycle re-entry for treating or preventing Alzheimer's disease in a human.

(3) Guidance of the Specification /Working Examples:

In the instant case, no working examples are presented in the specification as filed showing how to prevent Alzheimer's disease in a patient in need of such treatment totally, absolutely, or permanently.

(4) State/predictability of the Art:

The relative skill of those in the art is high. However the predictability is low. "To prevent" actually means to anticipate or counter in advance, to keep from happening etc. (as per Webster's II Dictionary). It is well-known in the state of the art that the cause of Alzheimer's disease is multifactorial, that is, there are several factors whose combined effects produce Alzheimer's disease. Alzheimer's disease may result from age related changes, family history, inflammation in the brain etc. These conditions are caused by various etiologies. For example, Alzheimer's disease may be due to neuron loss in the central nervous system or due to deposition of beta-amyloid plaques in the brain. Thus by treating one condition such as reducing the neuron loss in the central

nervous system, one could not prevent Alzheimer's disease from occurring. The current known treatment of Alzheimer's disease depends on the patient populations and the severity of the disorder. The underlying cause of Alzheimer's i.e. what actually triggers the changes in the brain is still not known. It is likely that no single factor is responsible, but rather that it is due to a variety of factors, which may differ from person to person. Thus the skilled artisan would view that the prevention of Alzheimer's disease in a patient in need of such treatment totally, absolutely or permanently is unpredictable by administering compounds of formula I.

(5) The Quantity of Experimentation Necessary:

There is no working example provided for the prevention of Alzheimer's disease totally, absolutely or permanently. Therefore, Applicant fails to provide information sufficient to practice the claimed invention, absent undue experimentation. *Genetech*, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the *Wands* factors, e.g., the amount of direction or guidance provided, absence of working examples, and the predictability of the art discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation to test the combination in the instant claims whether preventing Alzheimer's disease totally, absolutely, or permanently.

Accordingly the claims are evaluated as a method of treating Alzheimer's disease and not method of preventing Alzheimer's disease.

Claims 5, 6, and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while enabling for the treatment of a subject who has Alzheimer's disease with the administration of a compound of formula I, does not provide sufficient information that the administration of a compound of formula I is capable of treating the wide array of ailments as set forth in claim 5.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The specification does not provide sufficient information that a compound of formula I is capable of treating the wide array of ailments as set forth in claim 5.

The instant specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

(1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of

working examples; and (8) the quantity of experimentation necessary.

(1). The Nature of the Invention:

All of the rejected claims are drawn to an invention which pertains to a method of treating a subject who has or in preventing a subject from getting a disease or condition as those set forth in claim 5 with the administration of a compound of formula I. The nature of the invention is complex in that it encompasses the treatment of a wide array of ailments upon administration of a compound of formula I.

(2). Breadth of the Claims:

The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims are much broader than the enabling disclosure.

As is noted above, the scope of the claims are very broad. The disorders covered by the scope are: neurodegenerative disorders, e.g. Alzheimer's disease; Down's Syndrome, Hereditary Cerebral Hemorrage with Amyloidosis of the Dutch type or other neurodegenerative or dementia-inducing disorders. Degenerative dementia includes all forms of dementia since dementia is the progressive decline of cognitive function due to damage or disease beyond normal aging. Dementia is a non-specific term that encompasses many disease processes, just as fever is attributable to many etiologies, e.g. Alzheimer's disease, vascular dementia (including Binswanger's disease), dementia with Lewy bodies, frontotemporal lobar degeneration (FTLD, including Pick's disease), frontotemporal dementia, semantic dementia, progressive non-fluent aphasia,

Creutzfeldt-Jakobt disease, Huntington's disease, Parkinson's disease, HIV infection, head trauma, hypothyroidism, vitamin B 1 (thiamine) deficiency, Vitamin B 12 deficiency, Vitamin A deficiency, depressive pseudodementia, normal pressure hydrocephalus and tumors. Thus, the scope of the claims is huge.

(3). Guidance of the Specification:

The guidance given by the specification as to how effective the disclosed compounds of formula I are at treating the desired ailments is limited, with the exception of Alzheimer's disease.

(4). Working Examples:

Applicant provides examples of *in vitro* and *in vivo* assays for the treatment of Alzheimer's disease.

(5). State of the Art:

These diseases and disorders covered by the scope of diseases above cannot be treated generally by any one drug. These are all different diseases and disorders, which occur at different locations and by different modes of action in the body.
The skill level, for example, for Alzheimer's disease is considered low. Alzheimer's disease is an extraordinarily difficult disease to treat, and has been the subject of a vast amount of research, exceeded in recent years only by research into AIDS and cancer.

It is well-known in the state of the art that the cause of Alzheimer's disease is multifactorial, that is, there are several factors whose combined effects produce Alzheimer's disease. Alzheimer's disease may result from age related changes, family history, inflammation in the brain etc. These conditions are caused by various etiologies. For example, Alzheimer's disease may be due to neuron loss in the central nervous system or due to deposition of beta-amyloid plaques in the brain. Thus by treating one condition such as reducing the neuron loss in the central nervous system, one could not prevent Alzheimer's disease from occurring. The current known treatment of Alzheimer's disease depends on the patient populations and the severity of the disorder. The underlying cause of Alzheimer's i.e. what actually triggers the changes in the brain is still not known. It is likely that no single factor is responsible, but rather that it is due to a variety of factors, which may differ from person to person.

Note that some of the diseases listed in the scope of diseases are "umbrella" terms that are very broad in scope. Such as dementia, most forms are untreatable. Down's Syndrome is a genetic disorder, which cannot be treated with pharmacological drugs.

(6). Nature and predictability of the invention:

The nature of the invention is directed towards medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological

activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(7). The Quantity of Experimentation Necessary:

In order to practice the claimed invention, one of skill in the art would have to first envision a combination of an appropriate pharmaceutical carrier, a dosage for each compound as encompassed by "a compound of formula I", the duration of treatment, route of treatment, etc. and, in the case of human treatment, an appropriate animal model system for one of the claimed compounds. One would then need to test the combination in the model system to determine whether or not the combination is effective for treating the numerous ailments set forth in the instant claims. If unsuccessful, which is likely given the lack of significant guidance from the specification or prior art regarding the numerous ailments with any one compound, one of skill in the art would have to then either envision a modification of the first combination of pharmaceutical compound, compound dosage, duration of treatment, route of administration, etc. and appropriate animal model system, or envision an entirely new combination of the above and test the system again. Therefore, it would require undue, unpredictable experimentation to practice the claimed invention to treat any of the numerous ailments by the administration of one of the compounds of formula I.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague

intimations of general ideas that may or may not be workable."

Therefore, methods of treating the numerous ailments as set forth in claim 5 by administering a compound of formula I is not considered to be enabled by the instant specification.

Conclusion

Claims 1-6 and 20 are not allowed.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SAHAR JAVANMARD whose telephone number is (571) 270-3280. The examiner can normally be reached on 8 AM-5 PM MON-FRI (EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan can be reached on (571) 272-0629. The fax

phone number for the organization where this application or proceeding is assigned is 571-273-8300.

SJ

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER